

Mesenteric ischemia: an update

Franco Stagnitti¹, Andrea Stagnitti²

¹ Rome "Sapienza" University, Italy

² St. John the Baptist Rome Hospital, Italy

Abstract

Acute mesenteric ischemia (AMI) is a time-sensitive medical emergency, like ST-elevation myocardial infarction or stroke. Improved methods of diagnosis and treatment have allowed us to reduce the mortality associated with AMI and to cushion the impact of surgery on patients with AMI who are often fragile with multiple comorbidities. Biphasic contrast enhanced computed tomography scan with multiplanar reconstruction (MPR-CT) permits us to accurately identify the location, extent and type of intestinal lesion present and promptly select the most suitable treatment. When there is a high suspicion of AMI patients should be treated with fluid resuscitation, systemic anticoagulation and broad-spectrum antibiotics for sepsis. In order to reduce surgical stress for these patients who are often critically ill, percutaneous endovascular procedures have become the method of choice to treat arterial and venous embolism and thrombosis, either via direct intervention on the clot or continuous locoregional infusion of fibrinolytics and anticoagulants or, in patients with NOMI, vasodilators.

Emergency surgery should only be performed in patients with peritonitis. The primary goal of surgery for occlusive AMI should be intestinal revascularization, with or without the assistance of interventional radiology, and only non-viable segments of the intestine should be resected.

Keywords: mesenteric ischemia; mesenteric infarction; vascular emergencies

Introduction

Acute mesenteric ischemia (AMI) is due to a sudden interruption of blood flow to part of the small intestine. If not treated rapidly it causes cell damage, intestinal necrosis and ultimately patient death.

AMI can be occlusive or non-occlusive (NOMI). Occlusive AMI most commonly occurs due mesenteric arterial embolism (50% of cases), mesenteric arterial thrombosis (15-25% of cases) or mesenteric venous thrombosis (5-15% of cases).[1]

The overall incidence of AMI is low (0.09% t-0.2% of all acute admissions to emergency departments) but there has been a modest increase in recent years. Although only ca. 1.1% of all patients admitted for acute abdomen have AMI, in patients over the age of 70 the incidence reaches 10%, with no significant difference between men and women.[2] The increasing incidence of AMI recorded in recent years seems to be due to an aging general population with a greater number of comorbidities that that adversely affect prognosis [3]

The mortality rate for AMI which used to be very high, 50-80%, has fallen in the past 15 years thanks to the

increasingly frequent use of endovascular techniques as well as to improvements in the management of critically ill patients in general and particularly patients with heart disease [4]

However, AMI remains a diagnostic challenge especially because of the difficulty in recognizing the condition before intestinal infarction occurs. The literature on AMI mainly consists of reviews and retrospective case series, often with small numbers of patients.

Corresponding author: Franco Stagnitti: franco.stagnitti@gmail.com
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Pathophysiology and clinical presentation of AMI

At rest the splanchnic circulation receives about 25% of the total cardiac output and postprandial splanchnic circulation can be as high as 35%. The intestinal mucosa and submucosa receive 70% of the mesenteric blood flow and in case of ischemia microscopic changes can be identified within minutes.[5] Although the intestine can survive a 75% reduction in blood flow for up to 12 hours without significant damage, complete, acute interruption of blood flow leads to irreversible mucosal ischemia within 6 hours. This causes a rapid reduction of cellular adenosine triphosphate levels, leukocyte infiltration, and the formation of oxygen free radicals, followed by the collapse of mucosal barriers, bacterial translocation and gangrene of the intestinal wall and subsequently peritonitis, ileus, sepsis and multiorgan insufficiency.[6]

AMI due to arterial embolism most frequently involves the superior mesenteric artery (SMA) probably because of its oblique origin from the abdominal aorta and higher flow. The occlusion usually occurs 3-10 cm distal to the origin, and beyond the origin of the middle colic artery and as a result the duodenum and transverse colon are spared. Only ca 15% of the emboli are found at the origin of the SMA.

If the occlusion is due to arterial thrombosis, it is usually superimposed on pre-existing atherosclerotic disease. Atherosclerotic lesions are most frequently found at the origin of the mesenteric arteries and therefore cause ischemia of a larger area of the intestine.

The predominant arterial occlusive lesion responsible for AMI is nearly always at the SMA, and is accompanied by occlusive disease of the celiac axis and inferior mesenteric artery (IMA). The multi-vessel involvement explains the fact that in AMI due to SMA thrombosis these lesions are often associated with other manifestations of atherosclerosis such as coronary artery disease and the patient may have a history of abdominal angina. [7,8].

Occlusion caused by venous thrombosis can result from thrombophilia such as factor V Leiden, Protein S or C or antithrombin III deficiency, or antiphospholipid antibody syndrome. In 70-95% of cases the thrombus lodges in the superior mesenteric vein but the inferior mesenteric vein and the portal axis can also be involved. [9]

NOMI, which constitutes 5-15% of the cases of mesenteric ischemia, is caused by intestinal hypoperfusion without vascular occlusion, and is associated with the highest in-hospital mortality rate because patients generally have multiple comorbidities often involving decreased sensation which makes diagnosis more difficult [8,10].

Clinically the initial phase of NOMI is characterized by acute, crampy, abdominal pain, with a pain-free interval

after 3-6 hours due to reduced activity of the intramural pain receptors as a result of prolonged hypoperfusion of the intestinal wall. Many studies report up to 20% of patients without abdominal pain and others who present with signs of peritonitis. [11]. In AMI 90% of patients have severe abdominal pain out of proportion to physical examination which has a sudden onset in cases of embolism and develops more slowly in other cases, and which migrates as the ischemia evolves. Other symptoms associated with AMI are nausea in 44% of patients, vomiting in 35%, diarrhea in 33%. Fecal occult blood is detected in 16% of AMI patients. Transmural infarction is often accompanied by bloody diarrhea.

In these more advanced phases of AMI, septic shock may develop. [12].

Diagnosis

AMI is a time-sensitive medical emergency: a delay in diagnosis has disastrous results. A high index of suspicion and prompt management are essential for preventing the negative effects of ischemia. The mortality associated with AMI has remained high for so many years because of the delay in recognizing and treating this condition: on average 7.9 hours until diagnosis, and another 2.5 hours before achieving mesenteric reperfusion.[2]. In a study on risk factors for mortality in patients with AMI, the mortality rate in patients operated on within 24 hours after symptom onset was 10.6% but rose to 72.9% if surgery was performed after 24 hours.[13] There may be clues in the patient's history. Patients with mesenteric arterial embolism are often young and have atrial fibrillation whereas those with arterial thrombosis tend to be older and have abdominal angina. Patients with mesenteric venous thrombosis are usually young with a history of thrombophilia and thrombophlebitis. Critical cardiovascular disease is common in patients with NOMI. It is also useful to know if the patient has recently undergone any surgery or invasive procedures involving vascular manipulation. AMI, specifically ischemia due to mesenteric venous thrombosis, can be a complication of any abdominal surgery, and other interventions such as colonoscopy, hypoperfusion, or coronary angiography can also set off AMI. [14,15]

Once there is a high suspicion of AMI it is important to avoid using inappropriate diagnostic procedures that are time consuming and do not provide accurate and or specific findings. No laboratory tests are specific enough for AMI. So far, no serological biomarkers for AMI have been identified. High serum levels of D-dimer and lactate are not specific for AMI even though they can be a useful diagnostic tool, especially in the early phases of AMI [10]

It has been shown that a rise in arterial lactate levels, especially within 24 hours after diagnosis, is associated with a negative outcome.[16]. If acute occlusion is suspected the investigation of choice is biphasic contrast enhanced computed tomography scan with multiplanar three-dimensional reconstruction (MPR-CT). MPR-CT imaging must include the entire abdomen in two phases and the contrast agent must only be administered intravenously not orally. MPR-CT is essential for diagnosing both arterial obstruction and venous thrombosis, is easily available, inexpensive, and the associated radiation exposure has been reduced. Aside from examination of the abdominal wall, the main advantage of MPR-CT compared to catheter angiography, which has lost its appeal, is its ability to rule out other pathologies in the differential diagnosis of AMI. The sensibility and specificity of MPR-CT are 93% and 100% respectively and the positive and negative predictive values are 94-100%. [2]. The distension of the intestinal loops makes ultrasound imaging useless and magnetic resonance imaging, although theoretically useful is less widely available and more complex than MPR-CT. If NOMI is suspected, the first step is catheter angiography, especially in patients on chronic dialysis, patients who have had recent cardiac surgery with extracorporeal circulation (0.5-1 of all cardiac surgery) or endoaortic balloon treatment, and those with a severely reduced cardiac output.[17]. Catheter angiography permits selective locoregional infusion of vasodilators and anticoagulants and the catheter can be left in place, facilitating angiographic follow-up to monitor the effects of treatment.

Initial approach

AMI is a vascular emergency and should be accorded the same degree of urgency as myocardial infarction or stroke. If it is treated early the associated mortality rate is less than 30% but if treatment is started more than 6-8 hours after symptoms appear the associated mortality rate can be as high as 50-60% and it reaches 80-100% if treatment is delayed more than 24 hours. [10,13,18], . Time until diagnosis and treatment is therefore a predictive factor for the progression of ischemia, together with patient age, existing comorbidities, and the location of the ischemic area and the etiology. It is clear that a peripheral location is associated with a better prognosis. As regards etiology, NOMI has a markedly better prognosis than occlusive forms of AMI [2]

In the initial phase of treatment, assessment of prognosis is a very important, although often undervalued step. The rules about informed consent as well as general medicolegal principles require that the prognosis is clearly indicated in the patient's chart, but this is not always done. [7]

As soon as a diagnosis of AMI is made intensive therapy should be initiated. First hemodynamic stability should be restored, since displacement of fluid volume towards the ischemic part(s) of the intestine and the general disintegration of the endothelium occur rapidly (within a

few hours) causing hypovolemia and interstitial leakage. Continued leakage can cause intra-abdominal pressure to rise and an intra-abdominal pressure of 10mmHg can already cause a notable reduction in portal blood flow. At ca 20 mmHg hepatic arterial flow is also reduced and pathophysiological mechanisms are triggered which, together with bacterial translocation and subsequent sepsis, lead to multiorgan failure. [10,19]

These patients often have acidosis, hyponatremia and coagulation abnormalities which should be corrected quickly. Stabilization of the patient includes fluid resuscitation with crystalloids, carefully monitored to avoid capillary leakage, frequent monitoring of lactate clearance, and central venous oxygen saturation, as surrogate measures of cardiac output. Viscoelastic tests (TEG® or ROTEM®) should be used to evaluate coagulation and guide administration of hem components and hem derivatives. [20]

To prevent worsening of the thromboembolic occlusion patients should immediately receive anticoagulant therapy, 5000 IU of heparin administered as an intravenous (IV) bolus, followed by a continuous IV infusion of ca.20,000 IU of heparin/24 hours. Moreover, it has been shown that heparin therapy provides extremely good results in cases of venous occlusion whereas it is less successful in arterial AMI.[16] Treatment with antibiotics (for instance a second-generation cephalosporin plus metronidazole) must also be started immediately [2,21].

Current trends in treatment

Predictive factors of AMI progression influence the choice of treatment. One factor is time: if clinical signs of peritonitis are present, further investigations are useless and a waste of precious time. With immediate surgery it is possible to reduce the risk of systemic sepsis and in many cases to limit the extent of intestinal resection. Minimum remaining intestinal lengths must be respected in order to avoid short bowel syndrome.

In these cases, the current approach is to use the strategy of damage control surgery (DCS). The decision to use DCS must be made at an early stage based on the patient's response to resuscitation and their physiological status, because DCS is associated with improved survival [22,] Moreover, advanced age is not a contraindication to DCS since good results have been observed in old patients [22,23]

Since there is often uncertainty about intestinal viability, the intestinal stumps should be kept free and re-examined after the patient has been in the intensive care unit for some time and has been stabilized. The intestine is frequently "borderline" ischemic at initial exploration but improves after blood flow has been re-established and hemostasis restored.[24] Moreover, the intestine of these patients is often edematous and there is a high risk of anastomotic leak. Recent studies suggest that in these cases careful manual suturing is preferable to stapling. [25]

Various techniques for temporary abdominal closure after damage control laparotomy have been developed. Abdominal closure with a negative pressure device (negative -pressure wound therapy: NPWT) is the most commonly used technique. The open abdomen procedure can reduce the risk of abdominal compartment syndrome in patients who require prolonged resuscitation.[7]

Decisions about anastomosis, stoma or additional resection can be made at the same time as plans for sequential abdominal closure. Continuous fascial traction is a useful technique for delayed fascial closure.[23]

In occlusive ischemia surgical treatment should be guided by the principle of arterial reperfusion before consideration of intestinal resection.

Revascularization should always be attempted and involves exposure of the SMA by dissecting it free from the surrounding mesenteric tissue. If there is uncertainty about the diagnosis, arteriogram is the imaging modality of choice and can be performed intraoperatively especially in hybrid operating rooms.[26]

Various techniques can be used to restore blood flow, depending on the type of obstruction. Embolectomy and primary angioplasty or patch angioplasty are well established as definitive treatment for mesenteric artery embolism. Thrombosis of the SMA at its origin from the aorta (which is common in patients with diffuse atherosclerosis) requires a bypass procedure.

If there is any doubt about the viability of the intestinal stumps, they should be kept free so that follow-up endoscopy can be performed [2,21] or in some cases second-look laparoscopy, to evaluate intestinal viability.[27]

Because of the high number of comorbidities in AMI patients (whose average age is over 68) and the risks associated with open vascular reconstruction, the use of endovascular techniques has increased. Provided the patient does not have intestinal necrosis or peritonitis, percutaneous techniques using transfemoral or trans axillary access should be favored over open vascular reconstruction.[28]

Endovascular treatment includes aspiration, embolectomy with angiography, and/or lysis of the embolus with continuous locoregional transcatheter infusion of fibrinolytics or anticoagulants. To increase the contact of the clot with the drugs it can be fragmented using a guide wire. If there is thrombosis induced by atherosclerosis, percutaneous angioplasty of the SMA with stent placement can be performed. [7,10]

If the abdomen is open retrograde catheterization of the peripheral SMA with intervention in the central segment can be performed [29]

In cases of venous thrombosis, the technique of choice to prevent intestinal necrosis is recanalization using transhepatic trans jugular access, possibly placement of a trans jugular intrahepatic portosystemic shunt (TIPS) and subsequent locoregional fibrinolytic therapy.

If the portal vein is involved endovascular recanalization is always recommended even if the patient presents weeks

after the acute event and the intestinal perfusion appears to be adequately compensated, in order to prevent complications due to portal hypertension, in particular gastroesophageal varices [30,31].

In patients with NOMI endovascular procedures should be used for rapid selective transcatheter infusion of vasodilators into the SMA. Follow-up angiography is used to confirm the efficacy of the treatment.

Surgery is only required in patients with peritonitis or intubated patients with multiorgan dysfunction and only the parts of the intestine that are irreversibly damaged should be resected [10,21].

Conclusions

AMI remains a very serious condition associated with a high mortality rate in spite of improvements in diagnosis and treatment made in recent years. Since AMI is a vascular emergency, like myocardial infarction, time is a key factor. Early diagnosis and intervention are crucial for a favorable prognosis.[2]

The first steps taken when the patient arrives in the emergency room are of key importance for the patient's outcome. A recent retrospective study showed that early surgical assessment in the emergency room reduces intervention time by 5 hours, mean hospital stay by 4 days and mortality at 90 days by 25%. [32]

Emergency biphasic contrast-enhanced CT scan, which identifies the location, type and extent of the lesion, has become the gold standard in evaluating AMI.

Endovascular procedures, together with intensive care measures, can in many cases effectively treat AMI, reducing the surgical stress for these patients who are already in critical condition, with multiple comorbidities.

Only patients with peritonitis should have immediate surgery. The procedure can be performed as DCS with NPWT for temporary closure. If the patient does not have severe sepsis the primary aim of the surgery should be intestinal revascularization, performed with either an open or endovascular technique, and only non-viable intestinal segments should be resected [2,10, 22, 23].

Conflict of Interest

Authors have no conflict of interest to disclose

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